

ITW

Atty. Dkt. No. 029488-0113

Applicant: Philippe ROUANET et al.  
Title: PREVENTION AND TREATMENT OF BREAST  
CANCER WITH 4-HYDROXY TAMOXIFEN  
Appl. No.: 10/734,638  
Filing Date: 12/15/2003  
Examiner: Unassigned  
Art Unit: 1615

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**  
**UNDER 37 CFR §1.56**

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Submitted herewith on Form PTO/SB/08 is a listing of documents known to Applicants in order to comply with Applicants' duty of disclosure pursuant to 37 CFR §1.56.

A copy of each non-U.S. patent document and each non-patent document is being submitted to comply with the provisions of 37 CFR §1.97 and §1.98.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.

**TIMING OF THE DISCLOSURE**

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits, and within three (3) months of the mailing date of the foreign search report.

**RELEVANCE OF EACH DOCUMENT**

The relevance of the foreign-language document is described in the present specification. An English translation of the foreign-language document is not readily available. However, the absence of such translation does not relieve the PTO from its duty to consider the submitted foreign language document (37 CFR §1.98 and MPEP §609).

Applicants respectfully request that any listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

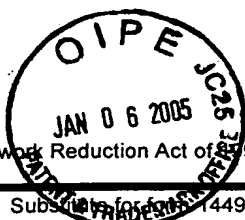
Respectfully submitted,

Date 6 January 2005

By S. A. Bent

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MODIFIED PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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Submittal for Form 1449B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

Date Submitted: January 6, 2005

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Sheet 1 of 3

**Complete if Known**

Application Number	10/734,638
Filing Date	12/15/2003
First Named Inventor	Philippe ROUANET et al.
Group Art Unit	Unassigned
Examiner Name	1615
Attorney Docket Number	029488-0113

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
	B1	5,904,930		Hexel AG	5/18/1999	

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
	B2	J. BARRAT et al., "Effet <i>in vivo</i> de l'administration locale de progestérone sur l'activité mitotique des galactophores humains", J. Gynecol. Obstet. Biol. Reprod. 19: 269-274 1990.	
	B3	Bronaugh & Maibach, "Percutaneous Absorption Drugs-Cosmetics-Mechanisms-Methodology", Marcel Dekker Inc., New York, 1999.	
	B4	Philip CARTHEW et al., "Cumulative exposure to tamoxifen: DNA adducts and liver cancer in the rat", Arch Toxicol (2001) 75: 375-380.	
	B5	Gerard CHETRITTE et al., "Effect of Promegestone, Tamoxifen, 4-Hydroxytamoxifen and ICI 164,384 on the Oestrone Sulphatase Activity of Human Breast Cancer Cells", Anticancer Research 13: 931-934 (1993).	
	B6	Eric C. DIETZE et al., "Tamoxifen but Not 4-Hydroxytamoxifen Initiates Apoptosis in p53(-) Normal Human Mammary Epithelial Cells by Inducing Mitochondrial Depolarization", The Journal of Biological Chemistry Vol. 276, No. 7, Issue of February 16, 2001, pp. 5384-5394.	
	B7	I.S. FENTIMAN et al., "Dosage and duration of tamoxifen treatment for mastalgia: a controlled trial", BR. J. SURG. September 1988, Vol. 75, No. 9, pp. 845-846.	
	B8	I.S. FENTIMAN et al., "Studies of tamoxifen in women with mastalgia", The British Journal of Clinical Practice, Supplement 68, Vol. 43, No. 11, November 1989, pp. 34-36.	
	B9	N. GIAMBIAGI et al., "IMMUNOLOGICAL DIFFERENCES BETWEEN THE ESTRADIOL-, TAMXIFEN- AND 4-HYDROXY-TAMOXIFEN-ESTROGEN RECEPTOR COMPLEXES DETECTED BY TWO MONOCLONAL ANTIBODIES", J. Steroid Biochem. Vol. 30, No. 1-6, pp. 213-217, 1988.	

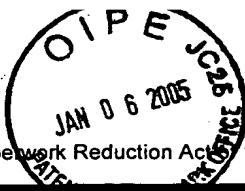
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Subsidiary Form 1449B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

Date Submitted: January 6, 2005

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Sheet 2 of 3

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Application Number	10/734,638
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First Named Inventor	Philippe ROUANET et al.
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	B10	V. Craig JORDAN et al., "Metabolites of tamoxifen in animals and man: identification, pharmacology, and significance", Breast Cancer Research and Treatment, 2, pp. 123-138.	
	B11	George G.J.M. KUIPER et al., "Comparison of the Ligand Binding Specificity and Transcript Tissue Distribution of Estrogen Receptors $\alpha$ and $\beta$ ", Endocrinology, Vol. 138, No. 3, 1997, pp. 863-870.	
	B12	Frédérique KUTTENN et al., "MÉDECINE ET THÉRAPEUTIQUE", C.R. Acad. Sc. Paris, , Série III, No. 12, 1985, 300:457-461.	
	B13	Catherine MALET et al., "Tamoxifen and Hydroxytamoxifen Isomers <i>versus</i> Estradiol Effects on Normal Human Breast Cells in Culture", Cancer Research, Vol. 48, No. 24, December 15, 1988, pp. 7193-7199.	
	B14	Pierre MAUVAIS-JARVIS et al., "trans-4-Hydroxytamoxifen Concentration and Metabolism after Local Percutaneous Administration to Human Breast", Cancer Research, Vol. 46, March 1986, pp. 1521-1525.	
	B15	David W. ROBERTSON et al., "Synthesis of the E and Z Isomers of the Antiestrogen Tamoxifen and Its Metabolite, Hydroxytamoxifen, in Tritium-Labeled Form", J. Org. Chem., 1982, Vol. 47, No. 12, pp. 2387-2393.	
	B16	David W. ROBERTSON et al., "TAMOXIFEN ANTIESTROGENS, A COMPARISON OF THE ACTIVITY, PHARMACOKINETICS, AND METABOLIC ACTIVATION OF THE C/S AND TRANS ISOMERS OF TAMOXIFEN" Journal of Steroid Biochemistry, Vol. 16, pp. 1-13, (1982).	
	B17	Fabrice SAUVEZ et al., "Cutaneously applied 4-hydroxytamoxifen is not carcinogenic in female rats", Carcinogenesis Vol. 20, No. 5, pp. 843-850 1999.	
	B18	Ashini L. WIJAYARATNE et al., "Comparative Analyses of Mechanistic Differences Among Antiestrogens", Endocrinology, Vol. 140, No. 2, pp. 5828-5840.	
	B19	"First results from the International Breast Cancer Intervention Study (IBIS-I): a randomized prevention trial", The Lancet, Vol. 360, September 14, 2002, pp. 817-824.	
	B20	Carsten SCHLÜTER et al. "The Cell Proliferation-associated Antigen of Antibody Ki-67: A Very Large, Ubiquitous Nuclear Protein with Numerous Repeated Elements, Representing a New Kind of Cell Cycle-maintaining Proteins", The Journal of Cell Biology, Volume 123, 1993, pp. 513-522.	
	B21	Debra J. BEVITT et al., "New Monoclonal Antibodies to Oestrogen and Progesterone Receptors Effective for Paraffin Section Immunohistochemistry", Journal of Pathology, Vol. 183, (1997) pp. 228-232.	
	B22	Lawrence H. BLOCK Ph.D., "Epidermal and Transdermal Drug Delivery", Medicated Topicals, Chapter 44, pp. 836-857.	
	B23	Corinne CHARLIER et al., "Tamoxifen and Its Active Metabolite Inhibit Growth of Estrogen Receptor-Negative MDA-MB-435 Cells", Biochemical Pharmacology, Vol. 49, No. 3, pp. 351-358, 1995.	

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Date Submitted: January 6, 2005		Filing Date	12/15/2003
(use as many sheets as necessary)		First Named Inventor	Philippe ROUANET et al.
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		Examiner Name	1615
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		Attorney Docket Number	029488-0113

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	B24	Ian S. FENTIMAN, "Tamoxifen and Mastalgia An Emerging Indication", Drugs 32 477-480 (1986), pp. 477-480.	
	B25	Johannes GERDES et al., "CELL CYCLE ANALYSIS OF A CELL PROLIFERATION-ASSOCIATED HUMAN NUCLEAR ANTIGEN DEFINED BY THE MONOCLONAL ANTIBODY Ki-67 <sup>1</sup> ", The Journal of Immunology, Vol. 133, No. 4, October 1984, pp. 1710-1715.	
	B26	J. GIRAULT et al., "Quantitative Measurement of 4-Hydroxy Tamoxifen in Human Plasma and Mammary Tumours by Combined Gas Chromatography/Negative Chemical Ionization Mass Spectrometry", Biological Mass Spectrometry, Vol. 22, (1993) pp. 395-402.	
	B27	Trisha GURA, "Cancer Models: Systems for Identifying New Drugs Are Often Faulty", Science, Vol. 278, November 7, 1997, pp. 1041-1042.	
	B28	Stanley G. KORENMAN et al., "ESTRADIOL RADIOIMMUNOASSAY WITHOUT CHROMATOGRAPHY: PROCEDURE, VALIDATION AND NORMAL VALUES", J. Clin. Endocrinol. Metab. 38:718-720 (1974).	
	B29	Catherine MALET et al., "Effect of 4-hydroxytamoxifen isomers on growth and ultrastructural aspects of normal human breast epithelial (HBE) cells in culture", Journal of Steroid Biochemistry & Molecular Biology 82, (2002) pp. 289-296.	
	B30	Catherine S. MURPHY et al., "Structure-Function Relationships of Hydroxylated Metabolites of Tamoxifen that Control the Proliferation of Estrogen-Responsive T47D Breast Cancer Cells In Vitro", Molecular Pharmacology, Vol. 38, No. 5, (1990), pp. 737-743.	
	B31	Mona NEMANI et al., "Activation of the human homologue of the Drosophila sina gene in apoptosis and tumor suppression", Proc. Natl. Acad. Sci. USA, Vol. 93, pp. 9039-9042, August 1996.	
	B32	Y. NOMURA et al., "Effects of antiestrogens and medroxyprogesterone acetate on the clonogenic growth of tamoxifen-sensitive and resistant human breast cancer cells", Japanese Journal of Cancer Chemotherapy, 12(4), pp. 844-850 (1985)	
	B33	Naushin H. WASEEM et al., "Monoclonal Antibody Analysis of the Proliferating Cell Nuclear Antigen (PCNA) Structural conservation and the detection of a nucleolar form, Journal of Cell Science, 96, 121-129 (1990).	

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